

Using Theater to Promote Understanding of the Immune System's Response to Viral Infection

Resource Type: Curriculum: Classroom

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Authors

Kim Risley
Mount Union College
Alliance, OH 44601
USA
Email: risleykm@muc.edu

Abstract

Using theater, students are led by peers into the world of a virus infection. Students actively participate in a play as narrator, props manager, actor, or audience member. The play is first performed as if a traditional viral infection has occurred. Students are posed questions pertaining to the immune response and what is happening to the virus. In a human immunodeficiency virus (HIV) extension activity, the students predict what will happen if HIV is the infectious agent. The play is re-run to visualize the outcome.

Activity

Description:

This activity allows students to demonstrate proficiency in understanding how the immune system responds to a viral infection such as with the human immunodeficiency virus.

Core Themes: Theme 3: Microorganisms and humans
Theme 6: Teaching and learning

Microorganisms Present: None used

Microbiology Keywords: AIDS, Antibodies, Antigen, Cytokines, Immune System, Infectious Disease, Viruses

Pedagogy Keywords: Assess, Learn, Teach, Active Learning

Science Discipline Keywords: Immunology, Microbiology, Virology

Audience:
Allied Health majors
Biology majors
Nonscience majors
Science education majors

Core Skills:
Thinking: Analysis
Thinking: Cognitive Process
Thinking: Communication

Learning Time: 1 hour

ACTIVITY

Learning Objectives.

Students will:

- learn the roles for the major cells involved in humoral and cell-mediated immune responses to a viral infection.
- be able to explain why both the humoral and cell-mediated responses are necessary to clear a viral infection.
- learn what happens to a virus during an immune response.

Background.

This activity is useful for students with basic knowledge on how the immune system functions. Students should be knowledgeable about basic virus and cell structure and the idea that viruses are obligate intracellular parasites.

PROCEDURE

Materials.

Materials can be duplicated to run multiple plays in the same classroom.

Virus—can make multiples per play to reflect viral replication!
· One 4-inch styrofoam ball

- 24 pipe cleaners, cut in half
- 48 brightly colored plastic beads
- Glue or hot glue gun

Directions: Glue one bead on one end of each pipe cleaner; insert pipe cleaners around styrofoam ball to represent virus spikes.

Immune cells and player name tags

- 8 ½" x 11" paper (one sheet per student)
- Masking tape
- Labels with the following written on them:
 1. Cell "The Host"
 2. CD4⁺ T cell "The Stimulator" (x2)
 3. Cytokines "The Signalers" (x2)
 4. Chemokines "The Recruiters"
 5. Macrophage "The Engulfer"
 6. CD8⁺ T cell "Pre-Attack Cell"
 7. Cytotoxic T lymphocyte (CTL) "The Attacker"
 8. B cell "The Humoralist"
 9. Plasma cell "Antibody Machine"

Props

- Plastic bag with several 1-inch styrofoam balls; "toxic granules" for the CTL
- Six hinged clothespins; "antibodies" for the plasma cell
- One pipe cleaner cut in half with a plastic bead glued to each end for "major histocompatibility complex (MHC) class I and antigen" (both for the infected cell)
- Two pipe cleaners (a different color than that for MHC class I) cut in half with a plastic bead glued to each end for "MHC class II and antigen" (two for the macrophage and two for the B cell)
- Two 6-inch pieces of pipe cleaner twisted together at the base and then shaped to form a Y; "T cell receptor (TCR)" for CD8⁺ T cell
- Four 6-inch pieces of pipe cleaner (of a different color than that for CD8⁺ TCR) twisted together in pairs at the base and then shaped to form a Y; "TCR" for CD4⁺ T cells

The Play "Much Ado about Infection"

- [Student version](#) (one copy per student)
- [Instructor version](#) (with supplemental information)

Instructor Version.

Classroom preparation.

Before the play:

- a. The class period before the play, assign the roles and have students learn about the characters. If doing the HIV extension, have all students answer these questions specifically for HIV as well.
 - i. Where do I "live"?
 - ii. What is my "job"?
 - iii. With whom do I typically "hang-out"?
- b. Make copies of the student version of the play (one per student) and assessment tool (two per student).
- c. Make copies (~20 minutes).

Some weblinks are included in the References portion of this activity for the instructor to review if necessary.

The day of the play:

- d. Have each student complete the preassessment self-report.
- e. Provide each student with a copy of the play.
- f. Have all props ready to hand out to their respective actors when directed.
- g. If you have a larger class (>20 students), you may want to set up multiple versions of the play to create more student engagement. For example, in a smaller class, you can make more cytokine sheets to include more students or let a student serve as narrator. For a class of 48, you can run the play simultaneously on two sides of the room with two identical sets of materials. You can have each class do the play twice and change the actors playing the roles so that each student has a chance to be in the play as well as be an audience member observing the play. Pausing after each scene allows for visual assessment of actor and prop placement.
- h. Have assessment tools ready. (Two copies of the survey per student if using the tool provided with this activity; one handed out before the activity and one after it.)
- i. Direct the play (and serve as the narrator or assign this to a student as well) and assign a student as the props manager. For nonmajor students, it may work best for you to be both the director and props manager with a student narrator at least the first time through the activity. Students like to share these roles as they gain more confidence with the activity and content.
- j. Notes to the director are included in ***bold italic*** font to the right of the script. These will aid in the direction of actors, use of props, and general placement on the stage, as well as provide answers to the student version questions.
- k. Have each student complete the postassessment self-report.
- l. Each student should turn in their script with the questions answered or answering the questions can be assigned as reflective homework to turn in during the next class period.

Safety Issues.

None

Suggestions for Determining Student Learning.

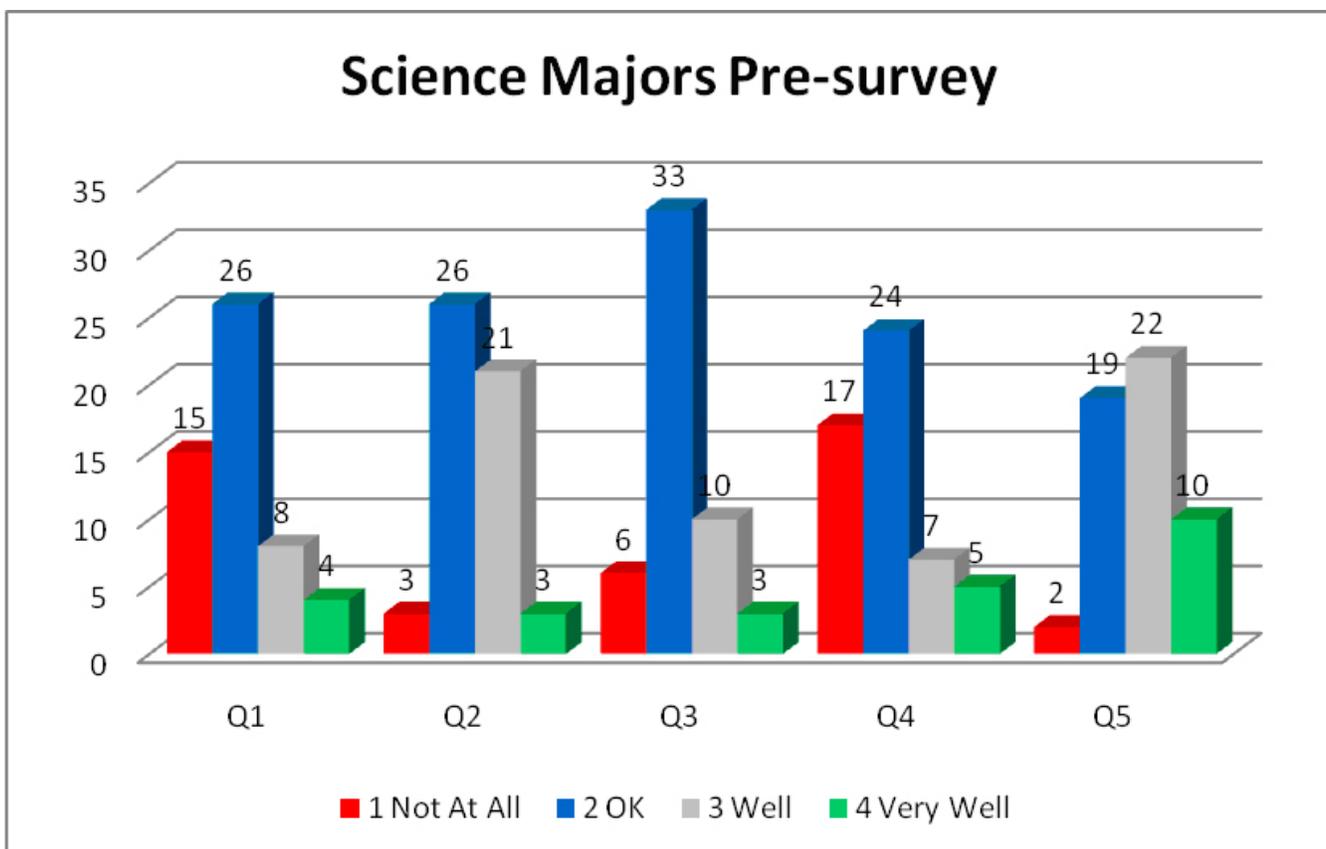
This activity is designed to be conducted in one 50-minute class period, however, discussions can take place during the following class meetings as well. This is also a good review tool before a summative assessment is administered. Formative assessments can include handing in the notes and questions, writing reflections in a journal, doing an assignment to further each student's understanding, or giving a pre- and postsurvey such as the one provided with this activity (Table 1). This in-class survey assessment gives immediate feedback to the instructor about areas which are still unclear to students.

TABLE 1. Student self-reporting pre- and postactivity assessment

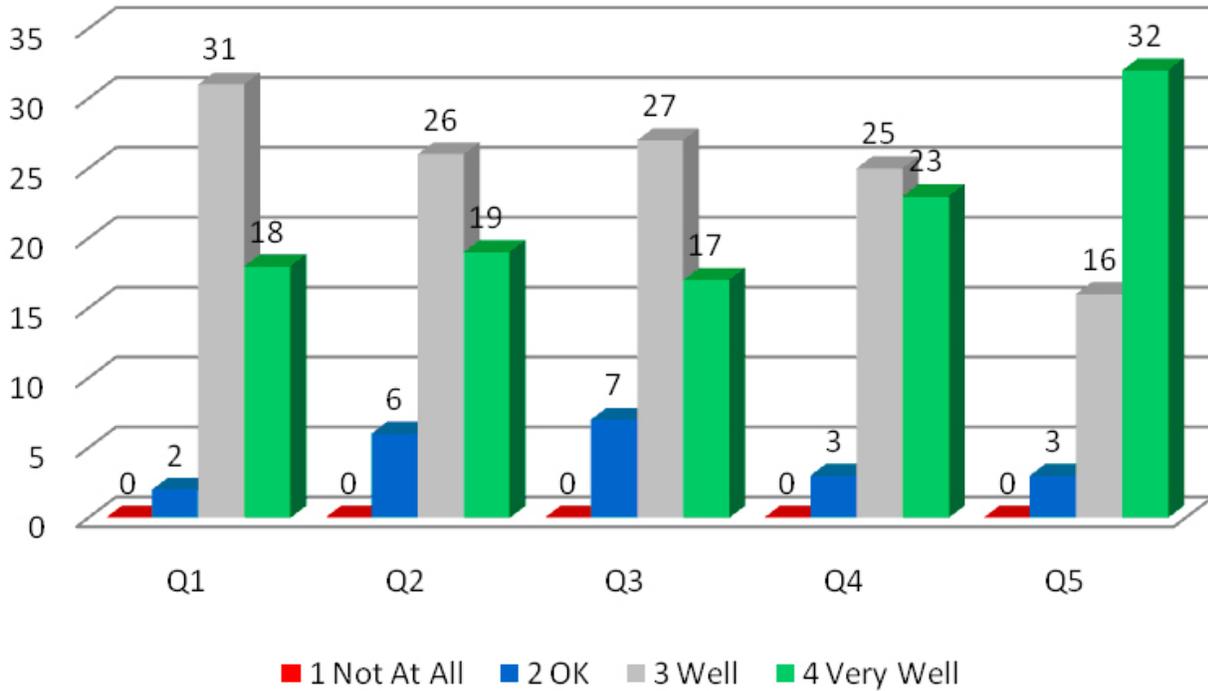
Question	Response			
	Not at all	OK	Well	Very well
Q1. I know how CD4 ⁺ T (helper) cells assist in an immune response.	1	2	3	4
Q2. I understand how antibodies affect viral infection.	1	2	3	4
Q3. I understand how cytotoxic T cells kill virus-infected cells.	1	2	3	4
Q4. I understand how HIV can affect CD4 ⁺ T (helper) cell activity.	1	2	3	4
Q5. I understand why HIV infection leaves a person vulnerable to other infectious diseases.	1	2	3	4

Science Major's Student Data

Responses to the survey questions (Q1 through Q5) for science majors are provided. Presurvey data is from surveys administered prior to the activity. Postsurvey data is from surveys collected following the activity. Majors include 53 respondents ($n = 53$) with three students having taken my immunology course the semester prior to this microbiology course. One did not respond to Q3 on the presurvey ($n = 52$), and two did not respond to the postsurvey ($n = 51$).



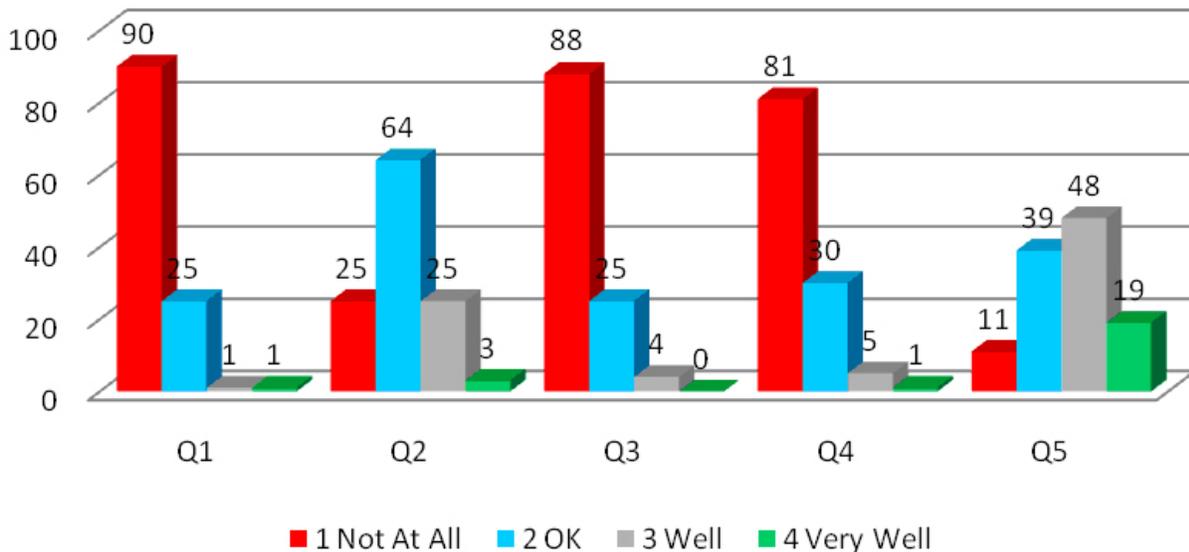
Science Majors Post-survey

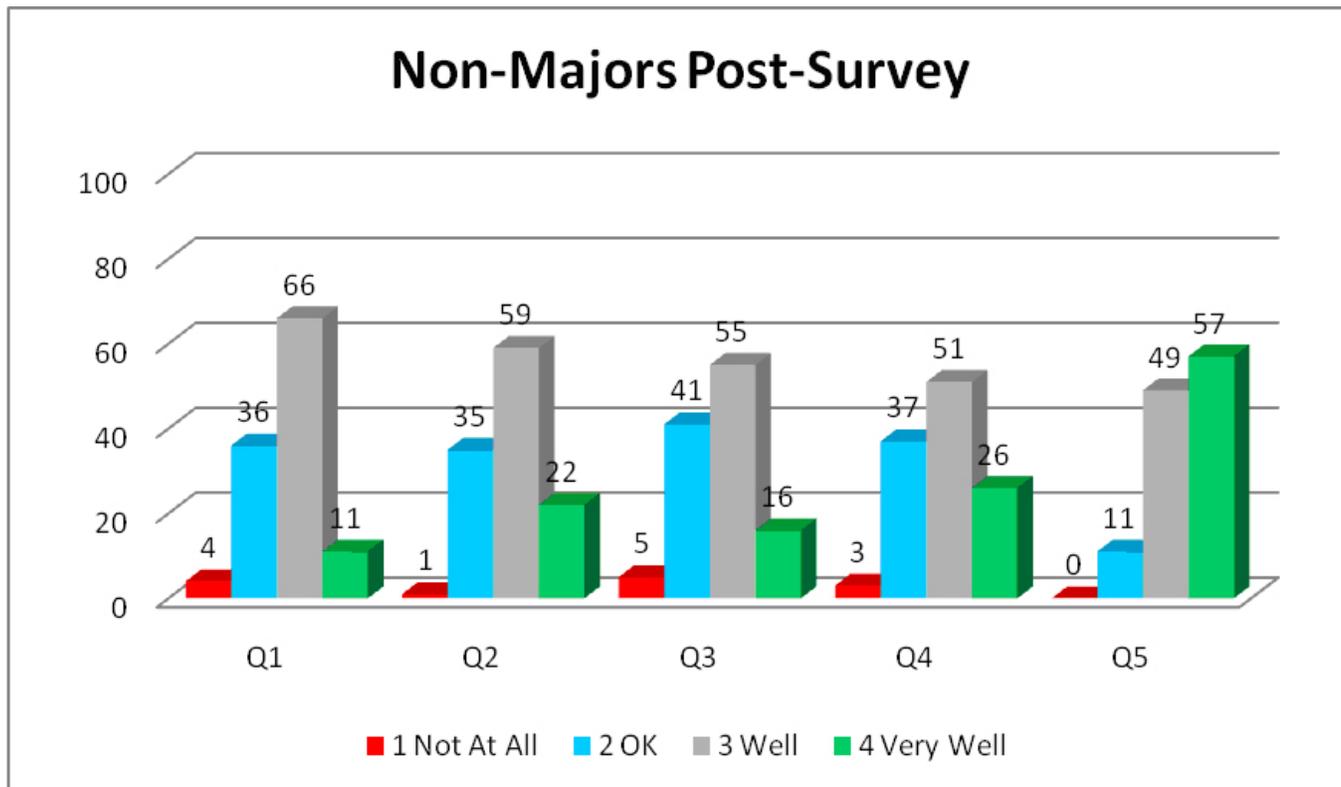


Nonmajor's Student Data

Responses to the survey questions (Q1 through Q5) for non-science majors are provided. Presurvey data is from surveys administered prior to the activity. Postsurvey data is from surveys collected following the activity. Non-science majors include 117 respondents ($n = 117$).

Non-Majors Pre-Survey





Field Testing.

This activity was initially created due to lack of student background in the fundamentals of how the immune system deals with a viral infection. Because many students may not have formal training in immunological responses before they enroll in an introductory microbiology course, it becomes difficult for students to truly comprehend how HIV impacts an individual's immune system. This activity has been used in introductory-level biology courses as well as in non-science major biology courses. It has been performed with less than 20 and close to 50 students. The activity can be repeated as many times as necessary to clarify student misconceptions or to "test" student hypotheses regarding the impact of HIV on the immune system. Likewise, the actors are also changed for a second rehearsal to give everyone a chance to both act and observe the interactions among the players. This activity gets students talking the lingo of an immune response without having to memorize definitions and then try to apply them. It also eases them into a fairly complex area of content without being intimidating due to their lack of prior knowledge. Students really get into their roles as the play unfolds and tend to identify with the role their cast member plays in an immune response. This activity allows for repetition and adaptability to different scenarios while still promoting student critical thinking skills each time it is used.

Assessments of learning objectives: In addition to student reporting, the following data were collected from student answers to course exam questions and address the objectives described.

Students will:

- learn the roles for the major cells involved in humoral and cell-mediated immune responses to a viral infection.
- be able to explain why both the humoral and cell-mediated responses are necessary to clear a viral infection.
- learn what happens to a virus during an immune response.

Science majors in an introductory microbiology course:

When asked "What is the difference between an antibody and an antigen?" 100% ($n = 19$) of the majors-level science students correctly characterized antibodies as protective and indicated that they are made in response to antigens; 21% specifically addressed the role of plasma cells in the generation of antibodies. (Objectives addressed: a, b) Sample answers included:

Student A: "Antigen is made by the virus and allows the immune system to recognize a foreign substance. An antibody is made by a plasma cell and is used to deactivate viruses by binding to the antigen, deactivating it, and marking it for degradation."

Student B: "An antibody is produced from B cells that have differentiated into plasma cells. They bind to antigens as an immune response. An antigen is a foreign invader of the body that signals the release of antibodies to fight it off."

"Mounting an effective immune response to HIV is difficult for several reasons. List two reasons why this is true." (Objectives addressed: a, b, c) Sample answers included:

Student A: "HIV lowers the number of CD4⁺ T cells, which release cytokines for both humoral and cell-mediated immune responses. Less CD4⁺ T cells leads to less signaling for response."

Student B: "Since these (CD4⁺ T) cells are a critical part of the specific immune response, it is even more difficult

for the immune system to fight HIV."

Student C: "It is difficult because HIV infects CD4⁺ cells, meaning those must be killed; however, they are extremely crucial to the effectiveness of the immune system."

Student D: "HIV targets a main contributor to the immune response, CD4⁺ T cells. This in turn doesn't allow them to signal for help to other immune cells and also continue in the immune response in releasing cytokines."

Students taking a nonmajors biology course:

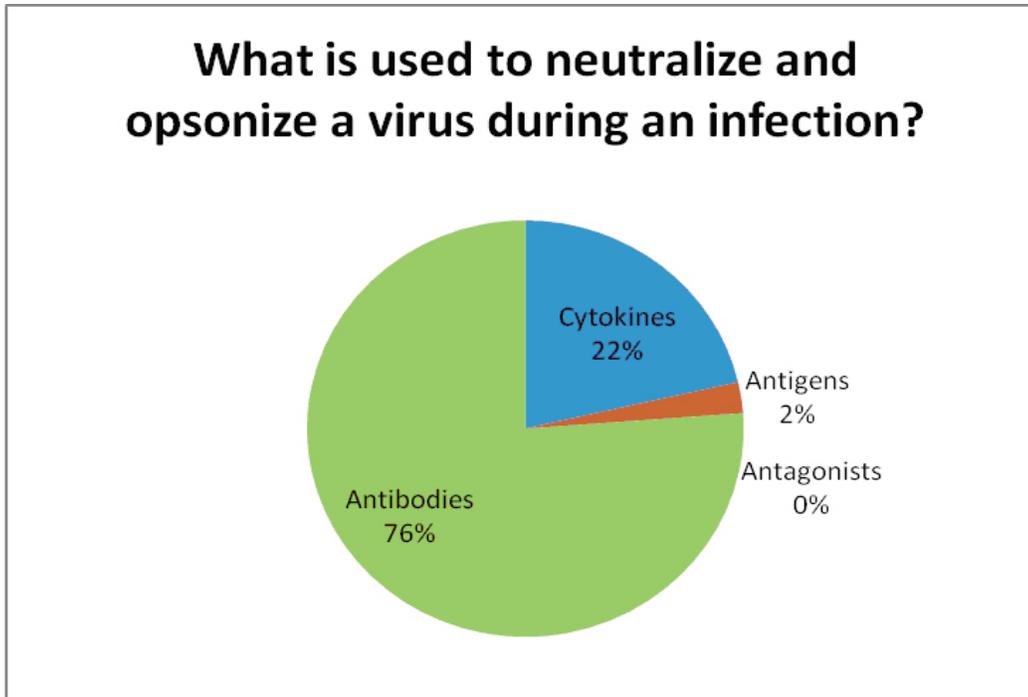


FIG. 1. In response to the question, 76% ($n = 42$) of non-science major students indicated that antibodies are used to neutralize and opsonize a virus during infection. (Objective addressed: c)

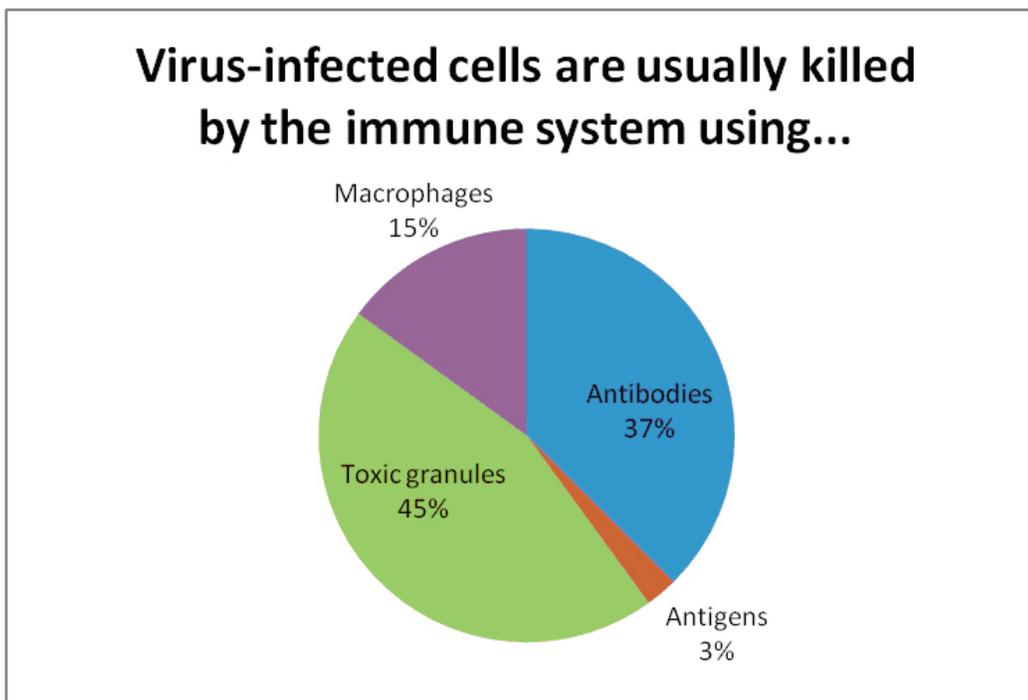


FIG. 2. Out of 40 non-science major students, 45% responded that virus-infected cells are usually killed by the immune system using toxic granules; 37% chose antibodies, 3% chose antigens, and 15% chose macrophages as a response. (Objectives addressed: a, b, c)

Additional resources.

The following websites provide helpful information regarding the immune system and HIV:

1. The body. The complete HIV/AIDS resource. <http://www.thebody.com/index/treat/immune.html> (multiple links about the immune system as well as HIV-specific information)
2. Immunity rules! Overview of the immune system. <http://microvet.arizona.edu/Courses/MIC419/Tutorials/immunityrules.html> (an immune system tutorial)
3. National Institute of Allergy and Infectious Diseases HIV/AIDS. <http://www3.niaid.nih.gov/topics/HIVAIDS/> (HIV-specific information)

Appendices.

- [The play "Much Ado About Infection" \(student version\)](#)
- [The play "Much Ado About Infection" \(instructor version\)](#)

Much Ado about Infection



The Cast: STUDENT VERSION

T cells: major players in cell-mediated immunity, regulators and effectors of the immune system, respond to antigen (Ag) fragments exposed on the surfaces of antigen-presenting cells (APCs), expressed on plasma membrane.

Subpopulations of T cells:

CD8+ cells

Role: “The Attackers”

CD4+ cells, also known as helper T cells

Role: “The Stimulators”

Macrophages: phagocytic cells and APC.

Role: “The Engulfers”

B cells: proliferate and differentiate into plasma or memory cells. Plasma cells respond to antigen by making and secreting antibodies (Ab). Memory cells “remember” the infectious agent and will differentiate into plasma cells during future exposure to the same Ag. They can act as APCs.

Role: “The Humoralists”

Virus: the infectious agent.

Role: “The Infector Gadget”

Host cell: an epithelial cell.

Role: “The Infectee”

Important Props:

Major histocompatibility

complex (MHC): assembled in endoplasmic reticulum.

Class I MHC: expressed by all cells except erythrocytes, bind and present internal peptides.

Role: “The Presenters” (Act 1)

Class II MHC: expressed by APCs involved in cell-mediated immunity (mainly macrophages, B cells, and other APCs), bind and present exogenous peptides.

Role: “The Presenters” (Acts 1 and 2)

Cytokines: secreted proteins.

Role: “The Signalers”

Chemokines: secreted proteins.

Role: “The Recruiters”

Antibodies: proteins made in response to antigen.

Role: “The Protectors”

Act 1. The Cell-Mediated Response STUDENT VERSION

Scene 1: The Recognition

<Enter virus, cell> Virus infects host cell.

Virus starts its replication cycle inside of the cell.

Viral proteins synthesized in the cytoplasm are degraded by proteasome complexes.

The viral peptides (Ag) are transported to the endoplasmic reticulum where they associate with class I MHC. The Ag-MHC complexes are then transported to the cell surface where CD8⁺ T cells recognize the peptide as foreign.

<Enter class I MHC with viral Ag on cell surface>

<Enter CD8⁺ T cells with T cell receptor>

CD8⁺ T cells recognize and bind the Ag-class I MHC complex via the T cell receptor (TCR). The CD8⁺ T cell needs several signals to become activated; one is binding the Ag-MHC class I complex. The other signal comes from the CD4⁺ T cell...

Scene 2: The Helper Cometh Forth!

<Enter macrophage and newly made virus>

Macrophage engulfs newly made virus, degrades the virus, processes its proteins, and presents them on the macrophage cell surface in association with class II MHC.

<Enter class II MHC with viral Ag>

<Enter CD4⁺ T cell with TCR>

The CD4⁺ T cell binds to MHC II-Ag complexes. The class II MHC-Ag-TCR interaction activates the CD4⁺ T cell, which then releases large amounts of cytokines to activate other cells.

Scene 3: The Killing Begins!

<Enter virus-infected cell, CD8⁺ T cell>

CD8⁺ T cells receive cytokine stimulation from activated CD4⁺ T cells (thus the name helper T cell), signaling the CD8⁺ T cell to differentiate into a cytotoxic T lymphocyte (CTL).

<Enter cytokines who “exchange” CD8⁺ T cell with CTL>

<Enter CTL with granules> The CTL kills the virus-infected cell by releasing toxic granules near the virus-infected cell.

<Exit all cast>

Notes and Questions

Why would a virus need to be inside a host cell?

Why is it important that the CD8⁺ T cell recognizes the Ag-MHC complex?

What two purposes does the macrophage serve during a viral infection?

Why would the CTL attack the virus-infected cell and not the virus itself?

Act 2. The Humoral Response STUDENT VERSION

Scene 1: The Recognition

<Enter macrophage with MHC II-Ag, CD4+ cell>

Meanwhile, the other CD4+ T cells recruited to the area also bind the MHC class II-viral Ag and become activated, releasing many cytokines.

<Enter chemokines who go and get the B cell>

<Enter B cell>

B cells also act as APC, presenting viral Ag on class II MHC.

<Enter class II MHC and viral Ag>

Scene 2: The Response

CD4+ T cells then interact directly with B cells by binding to the viral Ag-class II MHC complex on the B cell surface. These interactions cause B cell proliferation and differentiation into plasma cells; some cells remain as memory cells.

<Enter CD4+ T cells with TCR>

<Enter cytokines who “exchange” B cell with plasma cell>

<Enter plasma cell with antibodies>

Typically IgM is produced if this is the primary response to the virus.

Typically IgG is produced late in the primary response and during the secondary response to the virus.

The antibodies can bind to the virus and neutralize it, not permitting it to attach to any uninfected cells, or enhance phagocytosis of the virus by binding to its surface, thus marking it for degradation by phagocytes, a process called opsonization.

<End Act 2: Exit all cast>

The viral infection is now cleared, and the immune system has memory of this pathogen

to mount a quicker and more efficient response the next time it detects this virus!

THE END

Notes and Questions

A small amount of B cells become memory cells, which do not secrete Ab but will be ready to recognize the virus the next time it infects. Why would “memory” also be important for an immune response?

Why are the cell-mediated and humoral responses both necessary to clear the viral infection?

HIV extension activity **STUDENT VERSION**

But, with human immunodeficiency virus or HIV, this whole process doesn't go as smoothly as stated in this play. Why? Let's find out!

HIV can infect CD4+ T cells, macrophages, and other cells derived from macrophage precursors. HIV alters the function of these cells. Macrophages are one of the major reservoirs of HIV and allow the virus to be distributed to various tissues such as the brain and lungs.

In small groups, make a prediction about what the impact would be if CD4+ T cells were the cells being infected in the play.

Now re-run the play, this time inserting a CD4+ T cell as the original infected cell and HIV as the virus. What do you notice?

How does an HIV infection act differently than just a typical virus infection like in the play?

Instructor Version

A. Classroom preparation.

Before the play:

- a. The class period before the play, assign the roles and have students learn about the characters. If doing the human immunodeficiency virus (HIV) extension, have all students answer these questions specifically for HIV as well.
 - i. Where do I “live”?
 - ii. What is my “job”?
 - iii. With whom do I typically “hang-out”?
- b. Make copies of the student version of the play (one per student) and assessment tool (two per student).
- c. Make props (~20 minutes).

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- d. Have each student complete the preassessment self-report.
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Much Ado about Infection



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Role: “The Signalers”

Chemokines: secreted proteins.

Role: “The Recruiters”

Antibodies: proteins made in response to antigen.

Role: “The Protectors”

INSTRUCTOR VERSION

Page set-up: narrator reads left side.....director's cues on right side

Act 1. The Cell-Mediated Response

Scene 1: The Recognition

<Enter virus, cell> Virus infects host cell.
Virus starts its replication cycle inside of the cell.
Viral proteins synthesized in the cytoplasm are degraded by proteasome complexes.
The viral peptides (Ag) are transported to the endoplasmic reticulum where they associate with class I MHC. The Ag-MHC complexes are then transported to the cell surface where CD8⁺ T cells recognize the peptide as foreign.

<Enter Class I MHC with viral Ag on cell surface>

<Enter CD8⁺ T cells with T cell receptor>

CD8⁺ T cells recognize and bind the Ag-class I MHC complex via the T cell receptor (TCR). The CD8⁺ T cell needs several signals to become activated, one is binding the Ag-MHC class I complex. The other signal comes from the CD4⁺ T cell...

Scene 2: The Helper Cometh Forth!

<Enter macrophage and newly made virus>

Macrophage engulfs newly made virus, degrades the virus, processes its proteins, and presents them on the macrophage cell surface in association with class II MHC.

<Enter class II MHC with viral Ag>

<Enter CD4⁺ T cell with TCR>

The CD4⁺ T cell binds to MHC II-Ag complexes. The class II MHC-Ag-TCR interaction activates the T helper cell, which then releases large amounts of cytokines to activate other cells.

Scene 3: The Killing Begins!

<Enter virus-infected cell, CD8⁺ T cell>

CD8⁺ T cells receive cytokine stimulation from activated CD4⁺ T cells (thus the name helper T cell), signaling the CD8⁺ T cell to differentiate into a cytotoxic T lymphocyte (CTL).

Cell-cell killing

Allow virus to touch cell.

The cell's function is now to be a virus factory making more viruses.

This is how your immune system recognizes an infected cell.

Have student hold MHC-Ag (one per hand).

The TCR links with the MHC-Ag complex. These two cells remain linked together through Act I.

The macrophage is a "big eater" and kills the virus, taking pieces of it to present on Class II MHC.

Student holds one MHC-Ag in each hand.

These cells stay together.

Scan back to this infection.... How will we get rid of the infected cell (a virus factory)? By throwing toxic granules at it! 10

<Enter cytokines who “exchange” CD8+ T cell with CTL>

<Enter CTL with granules> The CTL kills the virus-infected cell by releasing toxic granules near the virus-infected cell.

<Exit all cast>

The infected cell tragically dies.

Act 2. The Humoral Response

Scene 1: The Recognition

<Enter macrophage with MHC II-Ag, CD4+ cell>

Meanwhile, the other CD4+ T cells recruited to the area also bind the MHC class II–viral Ag and become activated, releasing many cytokines.

<Enter chemokines who go and get the B cell>

<Enter B cell>

B cells also act as APC, presenting viral Ag on class II MHC.

<Enter class II MHC and viral Ag>

Antibody response

The B cell can also present viral antigen on Class II MHC. The interaction with the CD4+ T cell is similar to that with the macrophage.

Student holds one MHC-Ag in each hand.

Scene 2: The Response

CD4+ T cells then interact directly with B cells by binding to the viral Ag–class II MHC complex on the B cell surface. These interactions cause B cell proliferation and differentiation into plasma cells.

<Enter CD4+ T cells with TCR>

<Enter cytokines who “exchange” B cell with plasma cell>

<Enter plasma cell with antibodies>

Typically IgM is produced if this is the primary response to the virus.

The plasma cell should attach the antibodies onto the spikes of the virus. This neutralizes the virus—it can no longer bind to cell receptors effectively. Antibodies also opsonize the virus or tag it for degradation.

Typically IgG is produced if this is the secondary response to the virus.

The antibodies can bind to the virus and neutralize it, not permitting it to attach to any uninfected cells, or enhance phagocytosis of the virus by binding to its surface, thus marking it for degradation by phagocytes, a process called opsonization.

<End Act 2: Exit all cast>

Antibodies are big and bulky, not allowing spikes to bind to cell receptors for infection.

Macrophages love antibody-coated pathogens! Yum!

The viral infection is now cleared, and the immune system has memory of this pathogen to mount a quicker and more efficient response the next time it detects this virus! THE END

The immune system has killed the virus-making factory and the virus!

HIV extension activity—**INSTRUCTOR VERSION**

But, with human immunodeficiency virus or HIV, this whole process doesn't go as smoothly as stated in this play. Why? Let's find out!

HIV can infect CD4+ T cells, macrophages, and other cells derived from macrophage precursors. HIV alters the function of these cells. Macrophages are one of the major reservoirs of HIV and allow the virus to be distributed to various tissues such as the brain and lungs.

In small groups, make a prediction about what the impact would be if CD4+ T cells were the cells being infected in the play.

By infecting the CD4+ T cell, this cell is now a virus factory that doesn't function properly and is targeted for killing by the CTL. As this occurs, there are fewer and fewer CD4+ T cells to provide the "help" to immune cells in both the cell-mediated and humoral responses. A more detailed discussion could also include how HIV-infected cells can fuse with noninfected CD4+ T cells, resulting in syncytia formation and further reducing the CD4+ T cell counts and function.

Now re-run the play, this time inserting a CD4+ T cell as the original infected cell and HIV as the virus. What do you notice?

After the initial infection, the CD4+ T cell will be killed by the CTL. With only limited numbers of CD4+ T cell actors, it will become clear the immune system's response is impeded for both the cell-mediated and humoral responses.

How does an HIV infection act differently than just a typical virus infection like in the play?

As HIV infection progresses, instead of a better immune response and clearing of the infectious agent, the immune response weakens and HIV is prevalent.

Notes: this activity can serve as a springboard for discussion on how HIV patients are prone to infection by multiple types of infectious agents. This activity can easily be adapted for infections caused by bacteria, fungi, or parasites and can address items such as immune evasion or memory.